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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,649	07/28/2003	Lena Edelman	03495.0378-00	4213

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
06/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,649	EDELMAN ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,46,59,60,64-66 and 68-90* is/are pending in the application.

4a) Of the above claim(s) *35,59,60,64-66,68 and 85-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46 and 69-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

This action is responsive to communication filed 5/8/2009. The status of the claims is as follows: claims 46 and 69-84 are under current examination, claims 1-34, 36-45, 47-58, 61-63 and 67 are canceled, claims 35, 59-60, 64-66, 68 and 85-90 are withdrawn and claims 46 and 69-84 are under current examination. Claims 35, 46, 59-60, 64-66 and 68-90 are pending. Any rejection not reiterated herein has been withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/8/2009 has been entered.

Specification

The specification is objected to as it contains a multitude of nucleic acid and or amino acid sequences that lack their respective sequence identifier (i.e., SEQ ID NO:). Hence, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825,and applicants are requested to label all appropriate sequences with no additional new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 46 and 69-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6235872 (hereinafter as "Bredesen") in further view of US Patent No. 6713280 (hereinafter as "Huang"), and Roise and Schatz (*J. Biol. Chem.*, 1988)).

Bredesen discloses a chimeric, bifunctional protein comprising a proapoptotic peptide, including Bax, linked to a non-proapoptotic domain that imparts a second function such as facilitating cell entry (Abstract, col. 7, lines 19+, col. 1, lines 48+). Bredesen provides the tat peptide consisting of the sequence set forth by SEQ ID NO:

269 by the instant specification (col. 27, lines 31+, SEQ ID NO: 52). The author notes that attachment of this peptide fragment which facilitates cellular entry to the amino terminus of the proapototic peptide did not affect the function of the peptide to which it was linked. Proteolytic cleavage of the polypeptide is described and this may liberate an apoptotically active dependence domain that is accessible to the cellular apoptotic machinery (col. 4, lines 11+). Compositions comprising pharmaceutically acceptable carriers are described in col. 20, lines 28+.

Bredesen does not disclose the sequence set forth by SEQ ID NO: 239, use of D amino acids and C-terminal amide functions, a linker of 3-18 amino acids with a cleavage site and a chimera comprising an MLS (mitochondrial localization sequence) according to the formula of claim 46.

Huang describes peptide conjugates for the intracellular targeting of the Bcl-2, e.g. Bax, for modulating apoptosis (col. 4, lines 20+). The author characterizes apoptosis as the loss of mitochondrial function (col. 6. lines 1+). The author reveals the amino acid sequence set forth by SEQ ID NO: 239 (col. 10, Table 2) by the instant specification; see instant claims 72, 74, 78 and 80. Huang discloses the use of D amino acids (col. 7, lines 39+) as well as carboxy-terminus amidation (col. 7, lines 15+), meeting the limitation of a C-terminal amide function; see instant claims 73, 75, 77 and 81. The author also describes pharmaceutically acceptable vaccines for the delivery of the conjugates, including acceptable diluents (col. 17, lines 53+ and instant claims 69 and 82-84).

Roise and Schatz review mitochondrial sequences for the transport of fusion proteins to the mitochondria. The authors note that the mitochondrial targeting signal can be short as 12 amino acids and can function with different "passenger" proteins (p. 4509, col. 1). Further, the authors describe the proteolytic nature of the signal following transport to the mitochondria. Note that this signal meets an MLS (mitochondrial localization sequence) and all proteins are cleavable by one means or another. Separately, according to the formula of claim 46, an MLS may also serve and be interpreted as a linker. Thus, this reference provides a linker comprising of at least 12 amino acids with an MLS function.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a chimeric, bifunctional protein according to Bredesen and further include a Bax peptide (SEQ ID NO: 239) as taught by Huang. One would have been motivated to do so because for the advantage of modulating apoptosis. It would have also been obvious to include an MLS the advantage of specifically targeting the chimera or "passenger" protein to the mitochondria as taught by Roise and Schatz, given apoptosis takes place following loss of mitochondrial function (as taught by Huang).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 46 and 69-71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 76-81 and 85-95 of copending Application No. 10/059261 (PG PUB 2003/0077826). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a chimeric, bifunctional molecule with the formula of TARG-TOX wherein TARG includes SEQ ID NO: 269 or an HIV-1 tat fragment. Further, both sets of claims are drawn to D amino acids, a C-terminal amide function and peptide linkers.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is

(571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Gary B. Nickol /
Supervisory Patent Examiner, Art Unit 1646